UNITED STATES PATENT AND TRADEMARK OFFICE

C1C

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,188	11/21/2001	Birgit Jordan	2481.1761-00	9429

5487 7590 06/22/2005

ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,188	JORDAN ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *21-46 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/25/02; 4/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, claims 1-20 and 47, in the reply filed on April 14, 2005 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 21-46 and 48 are pending and withdrawn from consideration as being drawn to non-elected inventions. Claims 1-20 and 47 are pending and under examination.

Claim Objections

2. Claims 1 and 5 are objected to for reciting acronyms without spelling them out at their first occurrence in the claims. EVH1 represents Ena-VASP (*Drosophila melanogaster enabled* - vasodilator-stimulated phosphoprotein) Homology 1.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that monoclonal antibodies (mAb) IE245 and IE273 are required to practice the claimed invention because they are a necessary limitation for the success of the invention as

stated in the claims. As a required element they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the antibodies. See 37 CFR 1.802. The specification discloses that mAbs IE245 and IE273 have been deposited in a recognized deposit facility under the terms of the Budapest Treaty, however, if a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty **and** that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. (The second part regarding the removal of restrictions is lacking from Applicant's disclosure). See 37 CFR 1.808. In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

4. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a process for producing a product that has yet to be identified. Claim 47 is a reach through claim. To provide adequate written description and evidence of possession of a

claimed genus, a yet-to-be-discovered drug, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a function without any structural indications. There is not even identification of any particular class of chemicals that would have the disclosed function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

Therefore, claim 47 is not adequately demonstrated (described) possession of the unknown compound to be produced. Cancellation of claim 47 would overcome this rejection.

5. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As discussed above, the method of claim 47 produces an unknown compound. Applicant has not disclosed the identity of the compound (with the exception of its intended function), or how to make the claimed product. Without a disclosure of what compounds are useful for modulating the interaction between EVH1 and an EVH1 binding domain, one of skill in the art would not know how to make the claimed product. Cancellation of claim 47 would overcome this rejection.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claims 1-20 and 47 fail to recite complete method steps. In order for the claim to be understood, the method steps must conclude with a correlation step between the preamble of the claim the method steps. For example, step d) of claim 1 results in the

detection of labeled antibodies, but fails to correlate this step with a method of identifying a compound. A correlation step is required to overcome this rejection.

- Claims 5-11 recite, "VASP derivative" and "zyxin derivative", respectively. The metes and bounds of the identity of derivatives of VASP and zyxin are not discernable. It is unclear how altered the derivatives are in comparison to the original proteins, or what portions of the original protein are retained in the derivatives. The specification does not offer any further guidance on these terms. It is suggested that derivative language be removed in order to overcome this rejection.
- Claims 3, 4, 12-20 and 47 are unclear because a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 3 recites the broad recitation "consists essentially of", and the claim also recites "consists of" which is the narrower

statement of the range/limitation. Correction is required in order to overcome this rejection.

- Claim 20 recites, "identifying a medicament". The metes and bounds of this claim cannot be determined. The medicament is not correlated with the method from which the claim depends. Correction is required to over this rejection.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 12, 13 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gertler *et al.* (WO 98/01755, "Gertler"), in view of Reinhard *et al.* (*PNAS USA*, 92:7956-7960, 1995, "Reinhard") and Evangelista *et al.* (US 5,262,299, "Evangelista").

The claims are drawn to a process for identifying a chemical compound which modulates an interaction between an EVH1 binding domain (or a protein having said domain) and an EVH1 domain (or a protein having said binding domain). The process comprises the steps of bringing the two proteins in contact in the presence of the candidate compound, incubating the mixture with a primary and secondary labeled antibody that binds to either of the two proteins. Detection of the labeled antibody indicates that the antibody bound said EVH1 domain protein. The process takes place on a solid body, such as a microtiter plate coated with the EVH1 binding domain protein. In particular embodiments, the protein having the EVH1 domain is VASP of a

vertebrate, specifically human VASP. The protein having the EVH1 binding domain is zyxin, specifically human zyxin. VASP binds zyxin. Also claimed are polyclonal and monoclonal antibodies in the incubation step of the process. In another embodiment, the antibody label is a radioactive isotope, a fluorescent dye or an enzyme, such as alkaline phosphatase, beta-galactosidase, lanthanide in a europium complex.

Gertler discloses a screening method for a modulator of a protein (*Mammalian Ena*, abbreviated "*Mena*") having an EVH1 binding domain that binds to EVH1 proteins such as zyxin and vinculin (abstract). In one embodiment, the modulator is a chemical compound (page 28, lines 28-32). Assays are disclosed suitable for high throughput screening assays designed to identify modulators of *Mena* or Ena-VASP-like (abbreviated *Evl*) expression and/or activity (page 23). In one embodiment, the protein is contacted with a binding partner in the presence of the candidate modulating compound. The protein and its binding pair will either complex or remain separate proteins. If a complex forms, the candidate has no modulation activity on the EVH1 protein or binding domain. If a complex does not form, then the candidate has modulation activity on the EVH1 protein and binding protein (page 23, lines 13 through page 24, line 19). Gertler discloses that secondary antibodies may be used to detect anti-EVH1 antibodies. The assays are conducted on solid phase (page 24, lines 24-29). Also disclosed are monoclonal and polyclonal antibodies that bind to proteins comprising EVH1 domains (page 17, lines 16-30). Further, the EVH1 domain protein is a fusion protein with glutathione S-transferase (page 24, lines 24-27). Gertler suggests the use of a solid phase for the assay, however, there is no teaching about a microtiter plate as claimed by Applicant. Gertler suggests the use of labels for the antibodies, however, there is no teaching regarding the types of labels.

Specifically, Gertler is silent on alkaline phosphatase or beta-galactosidase, and lanthanide in a europium complex.

However, Reinhard discloses as assay wherein a zyxin family member (p83) was coated to the surface of microtiter wells and human VASP was applied as a ligand (page 7956, column 2, first full paragraph, and page 7958, second column, first paragraph). Reinhard mentions that a human zyxin homologue was discovered (page 7959, first column, first full paragraph). Reinhard also discloses a double-label immunofluoresence assay monoclonal and polyclonal antibodies labeled with rhodamine and FITC (page 7958, second column, third full paragraph, and Figure 4 caption). Further, Evangelista discloses various labels used for detection assays. The labels include lanthanide chelate (europium complex), alkaline phosphatase and beta-galactosidase (Figures 1-13).

It would have been obvious to incorporate the teachings of Reinhard and Evangelista into the method of Gertler. One would have been motivated to perform the detection assay on a solid support, such as a microtiter plate, in order to test more candidate compounds. One would have had a reasonable expectation of success because Gertler suggest the use of a solid body, and Reinhard performs a similar assay to Applicant's assay with VASP and a zyxin family member. One would have been motivated to use the labels taught by Evangelista because Gertler suggests the use of labels for the antibodies. One would have been motivated to use Evangelista's label because Evangelista teaches that the lanthanide label is highly sensitive. As for beta-galactosidase and alkaline phosphate labels, these are common labels in the art of immunoassay, evidenced by Evangelista's Figures detailing several of the well-known labels in the art. Regarding the limitation of claim 13, wherein the monoclonal antibody is synthesized using

hybridoma cells, Gertler's monoclonal antibodies anticipate this limitation. Monoclonal antibodies are only ever produced from hybridoma cells to date. Regarding the use of human VASP and zyxin in the immunoassay, one would have been motivated to use human proteins in order to discover chemical compounds appropriate for human administration should any be found effective and safe. Therefore, the invention as a whole would have been *prima facie* obvious at the time of the invention.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

8. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
June 15, 2005